General

Guideline Title

Antiretroviral therapy.

Bibliographic Source(s)

New York State Department of Health. Antiretroviral therapy. New York (NY): New York State Department of Health; 2014 Jan. 129 p. [106 references]

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: New York State Department of Health. Antiretroviral therapy. New York (NY): New York State Department of Health; 2010 Sep. 112 p. [45 references]

Recommendations

Major Recommendations

The quality of evidence (I-III) and the strength of recommendation (A-C) are defined at the end of the "Major Recommendations" field.

Goals, Benefits, and Risks of Antiretroviral Therapy (ART)

Clinicians should prescribe an ART regimen that is best able to delay disease progression, prolong survival, and maintain quality of life through maximal viral suppression (see table below). (I)

The clinician should involve the patient in the decision-making process when determining whether to implement ART. The clinician should review the benefits and risks of treatment for each individual patient. (III)

Table: Goals of Antiretroviral Therapy

- Maximal and durable suppression of viral replication (measured by viral load assays)
- Restoration and/or preservation of immune function
- Reduced human immunodeficiency virus (HIV)-related morbidity and mortality
- Improved quality of life
- Limitation of the likelihood of viral resistance to preserve future treatment options

When to Initiate Art in Patients with Chronic Infection

Table: Recommendations for Initiating ART

Recommendations for Initiating Antiretroviral Therapy (ART)
1. All patients with chronic human immunodeficiency virus (HIV) infection should be evaluated for initiation of ART, regardless of CD4 count. (AII) 2. Certain conditions increase the urgency for initiation of ART. Clinicians should strongly recommend initiation of ART in patients who meet any one of the following criteria[a]: • Acquired immunodeficiency syndrome (AIDS)-defining condition (AI) • Pregnancy[b] (AI) • Two successive measurements of CD4 counts ≤500 cells/mm^3 (AII) • Symptomatic from HIV (AI), regardless of CD4 count, including any of the following: • HIV-associated neurocognitive disorder (HAND)[c] (AII) • Severe thrombocytopenia (AII) • HIV-associated nephropathy (AII) • HIV-related malignancies (AII) • Chronic hepatitis B or C infection[d,e] (AII) • Age 50 or older (AII) • Rapidly declining CD4 counts (>100 cells/mm^3 per year) (AIII) 3. Patients with seronegative partners should be counseled about the reduction of HIV transmission risk when effective ART is initiated; ART is strongly recommended in these patients. (AI)
[a]See Appendix C in the original guideline document for evidence and ratings. [b]For recommendations on initiating ART in HIV-infected pregnant women, refer to Use of Antiretroviral Therapy in HIV-Infected Pregnant Women. [c]HAND is currently used to encompass a hierarchy of progressive patterns of central nervous system involvement ranging from asymptomatic neurocognitive impairment (ANI), to minor neurocognitive disorder (MND), to the more severe HIV-associated dementia (HAD) (see Cognitive Disorders and HIV/AIDS). [d]Initial ART regimens for patients with chronic hepatitis B must include NRTIs that are active against hepatitis B (see the National Guideline Clearinghouse [NGC] summary of the New York State Department of Health AIDS Institute guideline Hepatitis B virus). [e]In co-infected patients with HCV genotype 1 and CD4 counts >500 cells/mm^3, some clinicians would defer ART until HCV treatment is concluded due to significant interactions between some antiretroviral agents and NS3/4A protease inhibitors used as part of hepatitis C therapy (see the NYSDOH AIDS Institute guideline Hepatitis C virus).

Evaluation and preparation for ART initiation includes each of the following essential components:

- Full discussion with the patient about risks and benefits of ART (see "Counseling and Education Before Initiating ART" below)
- Assessment of patient readiness
- Identification and amelioration of factors that might interfere with successful adherence to treatment, including inadequate access to medication, inadequate supportive services, psychosocial factors, active substance use, or mental health disorders

Clinicians should refer patients for supportive services as necessary to address modifiable barriers to adherence. An ongoing plan for coordination of care should be established.

Clinicians should involve patients in the decision-making process regarding initiation of ART. The patient should make the final decision of whether and when to initiate ART.

When the decision to initiate treatment is made, ART should be prescribed and monitored by, or in consultation with, clinicians who have experience in managing ART.

Key Point:

To be successful over time, initiation of ART is a process that involves both the selection of the most appropriate regimen for the individual *and* its acceptance by the patient with education and adherence counseling. All are critical in achieving the goal of durable and complete viral suppression.

The Clinical Education Initiative (CEI) Line provides primary care providers in New York State the opportunity to consult with clinicians who have experience managing ART. The CEI Line can be reached at 1-866-637-2342 or 1-585-273-2793.

The AIDS Institute maintains a voluntary HIV Provider Directory to assist with identification of experienced providers in New York State. Experienced providers can also be identified through the American Academy of HIV Medicine (AAHIVM) and the HIV Medicine Association (HIVMA).

See Appendix B in the original guideline document for a comparison of the recommendations on when to initiate ART from the New York State Department of Health AIDS Institute, the Department of Health and Human Services, and the International AIDS Society – USA Panel.

Counseling and Education Before Initiating ART

Counseling and education should include the following:

- Basic education about HIV, CD4 cells, viral load, and resistance
- Available treatment options and potential risks and benefits of therapy (see Table 4 in the original guideline document)
- The need for strict adherence to avoid the development of viral drug resistance (see "The Importance of Patient Adherence" below)
- Use of safer-sex practices and avoidance of needle-sharing activity, regardless of viral load, to prevent HIV transmission or superinfection

Clinicians should involve the patient in the decision-making process regarding initiation of ART.

Deferring ART

Except in cases when initiation of treatment is urgent (see "Initiating ART Following Acute Opportunistic Infections [OIs]" below), clinicians should educate and prepare patients before initiating ART in those with potential barriers to adherence, including low health literacy; active alcohol or drug use; lack of insurance, transportation, or housing; depression; mistrust of medical providers; or a poor social support system.

In patients with advanced HIV (or acquired immunodeficiency syndrome [AIDS]), ART should be initiated even if barriers to adherence are present. In these cases, referrals to specialized adherence programs should be made for intensified adherence support (see Appendix D: New York State Adherence Services Contact List in the original guideline document).

Decisions to initiate ART in long-term nonprogressors and elite controllers should be individualized. (AIII)

Long-Term Nonprogressors and Elite Controllers

Clinicians should consult with a provider experienced in the management of ART when considering whether to initiate ART in long-term nonprogressors and elite controllers.

Long-term nonprogressors demonstrate a lack of disease progression, marked by no symptoms and low viral loads in the absence of therapy during long-term follow-up. Most published studies of long-term nonprogressors include 7-10 years of follow-up.

Elite controllers suppress HIV to low but detectable levels (<50-75 copies/mL) for many years.

Initiating ART Following Acute Opportunistic Infections (OIs)

Clinicians should recommend that patients beginning treatment for acute opportunistic infections (OIs) initiate ART within 2 weeks (*see next recommendation for exceptions*). (AI)

Clinicians should not immediately initiate ART in patients with tuberculous meningitis or cryptococcal meningitis. Consultation with a clinician with experience in management of ART in the setting of acute OIs is recommended.

For all other manifestations of tuberculosis (TB), clinicians should initiate ART in HIV-infected patients as follows:

- *For patients with CD4 counts ≥50 cells/mm^3*: as soon as they are tolerating anti-TB therapy and no later than 8-12 weeks after initiating anti-TB therapy (AI)
- *For patients with CD4 counts <50 cells/mm^3*: within 2 weeks of initiating anti-TB therapy (AI)

The Importance of Patient Adherence

A team approach to achieving adherence should be used. Nurses, pharmacists, peer counselors, caseworkers, and others who work in outreach, evaluation, and support of adherence should be involved. (III)

The clinician should assess treatment readiness prior to initiation of treatment, adherence readiness for subsequent regimens, and adherence at every clinical visit. (III)

Interventions should be intensified in times of decreased adherence.

Information about patients' beliefs and attitudes should be communicated with all members of the healthcare team so that each provider can consistently address treatment adherence issues within the context of the overall treatment plan. (II)

If the patient is not fully committed to adhering to therapy, treatment should be delayed, and the clinician should continue to work on abating the patient's concerns. Appropriate referrals should be provided for support groups, mental health, and drug treatment. (III)

Refer to the original guideline document for the list of potential barriers to adherence and strategies for promoting adherence.

Selecting an Initial Antiretroviral Regimen

Clinicians should obtain genotypic resistance testing at baseline and should consider repeating the test prior to initiating treatment in ART-naïve patients. (AIII)

Clinicians should involve their patients when deciding which antiretroviral regimen is most likely to result in adherence. (AIII)

For ART-naïve patients, the initial preferred antiretroviral regimen should include a combination of two nucleoside/nucleotide reverse transcriptase inhibitors (RTIs) plus either a ritonavir-boosted protease inhibitor (PI), a non-nucleoside reverse transcriptase inhibitor (NNRTI), or an integrase inhibitor. (AI)

For women considering pregnancy or not using effective contraception, efavirenz or combination pills containing efavirenz should be avoided. If there are no alternatives for efavirenz in women of childbearing potential, clinicians should strongly advise the use of effective contraception and should obtain a pregnancy test before initiating treatment. (AI)

Selection of antiretroviral agents should be individualized to address each patient's concurrent morbidities and medications, ability to adhere to complex regimens, and personal tolerance for adverse medication effects. (AIII)

Clinicians should follow up with patients by phone or visit within 2 weeks of initiating therapy to assess tolerance and adherence to the antiretroviral regimen. Adherence should be reinforced at regular intervals during the course of therapy. (AIII)

Key Point:

The goal of the initial antiretroviral regimen is to achieve durable and maximal viral suppression (i.e., undetectable plasma HIV ribonucleic acid [RNA]) with minimal adherence challenges and long-term tolerability.

Refer to Tables 5-A and 5-B in the original guideline document for preferred and alternative ART regimens, respectively, for initial treatment of HIV infections and to Table 5-C for contraindicated and not recommended ART regimens for initial treatment of HIV infections.

See also Appendix A in the original guideline document for characteristics of antiretroviral drugs including specific dosing recommendations, including dose adjustments due to renal or hepatic impairment, adverse events, drug-drug interactions, and U.S. Food and Drug Administration (FDA) pregnancy categories for each antiretroviral agent.

Monitoring of Patients Receiving ART

Virologic and Immunologic Monitoring

- Routine quarterly monitoring of CD4 count is no longer recommended for non-pregnant patients receiving antiretroviral therapy (ART) who have consistently undetectable human immunodeficiency virus ribonucleic acid (HIV RNA) levels and CD4 counts >200 cells/mm^3 (see table below for recommended intervals). (AIII)
- Regular monitoring of HIV RNA levels remains the most meaningful measure of effective ART. (AI)

Clinicians should monitor HIV RNA levels and CD4 counts according to the recommended intervals in the table below.

In addition to recommended intervals for assessment of HIV RNA levels (see table below), clinicians should continue to schedule visits in accordance with clinical necessity to address any issues that may have an impact on adherence to ART or retention in care, such as substance use, mental health, unstable housing, lack of transportation, or social support, as well as non-HIV-related medical conditions. This may necessitate more frequent follow-up between monitoring visits. (AIII)

Key Point:

The table below provides a guide for monitoring HIV RNA levels and CD4 counts. Patients with a history of non-adherence, mental health disorders, substance use, homelessness, poor social support system, or other major medical conditions may need to be monitored more closely or may require more frequent visits.

Table: Virologic and Immunologic Monitoring

Virologic and Immunologic Monitoring*		
	Human Immunodeficiency Virus Ribonucleic Acid (HIV RNA) Levels (copies/mL)	CD4 Lymphocyte Count (cells/mm^3)
Baseline	Yes (AI)	Yes (AI)
Following initiation of antiretroviral therapy (ART) or change of ART regimen	• Within 4 weeks of initiation of ART or change in regimen (BIII) • At least every 8 weeks until complete suppression[a] is documented (BIII)	• At 12 weeks, then every 4 months until CD4 is ≥200 cells/mm^3 (AI) on two measurements obtained at least 4 months apart
Treatment Monitoring		
Patients on ART who achieve complete suppression	• At least every 3 months for one year after complete suppression (BIII) • May extend intervals to at least every 6 months in selected stable patients with CD4 count >200 cells/mm^3 after 1 year of complete suppression (Buscher et al., 2013) (BIII)	• At least every 6 months for patients with CD4 ≤300 cells/mm^3 (BIII) • At least every 12 months for patients with CD4 >300 cells/mm^3 (BIII)
Patients on previously suppressive ART with new HIV RNA[b] above the upper limit of a sensitive assay	Repeat viral load test within 4 weeks to differentiate low level transient viremia ("blip") from virologic failure.[c] If viral load remains detectable on repeat test: • Assess adherence (AIII) • Assess for drug-drug interactions (AIII) • Obtain resistance testing (AI) • Obtain CD4 count if not done within previous 6 months (BII)	
Patients not on ART (According to New York State Department of Health [NYSDOH] recommendations, all HIV-infected patients should be evaluated for initiation of ART.[d])	• At least every 4 months in patients with CD4 counts ≤500 cells/mm^3 (BIII) • At least every 6 months in patients with CD4 counts >500 cells/mm^3 (BIII) • Continue to discuss ART initiation (AIII)	• At least every 4 months for patients with CD4 ≤500 cells/mm^3 (BIII) • At least every 6 months for patients with CD4 counts >500 cells/mm^3 (BIII) • Continue to discuss ART initiation (AIII)

*For HIV-infected pregnant women, CD4 count and HIV RNA level should be monitored at baseline, within 4 weeks after initiating or changing ART, and every 3 months during pregnancy (at least once in each trimester). HIV RNA level should be obtained between 33 and 36 weeks' gestation to evaluate the need for elective cesarean delivery if HIV RNA level is elevated (>1,000 copies/mL) and to allow time to change the ART regimen, if indicated, before delivery.

[a]Complete suppression is generally considered below the level of quantitation of a highly sensitive assay (<20 to <50 copies/mL).

[b]Patients with repeated intermittent low level viremia <200 copies/mL over a period of years without demonstrated failure may continue routine testing intervals.

[c]ART should not be changed based on a single viral load elevation. The risk of virologic rebound (breakthrough) increases when values are >500 copies/mL.

[d]See "When to Initiate ART in Patients with Chronic Infection" above.

Key Point:

For HIV-infected pregnant women, CD4 count and HIV RNA level should be monitored at baseline, within 4 weeks after initiating or changing ART, and every 3 months during pregnancy (at least once in each trimester). HIV RNA level should be obtained between 33 and 36 weeks' gestation to evaluate the need for elective cesarean delivery if HIV RNA level is elevated (>1,000 copies/mL) and to allow time to change the ART regimen, if indicated, before delivery.

HIV Resistance Assays

Clinicians should perform resistance testing under the following circumstances:

- At baseline, regardless of whether ART is being initiated (genotypic testing)
- In ART-naïve patients before initiation of ART (genotypic testing) (III)
- In patients experiencing treatment failure or incomplete viral suppression while receiving ART (genotypic and/or phenotypic testing) (I)

When resistance testing is indicated, it optimally should be performed while patients are either receiving therapy or have been off therapy for less than 1 year. (III)

Clinicians should consult with an expert to interpret the results of resistance assays because the results of resistance assays are often complex (see Clinical Education Initiative sites available for phone consultation). (I)

Key Point:

Resistance testing more reliably indicates drugs that are not likely to be effective rather than identifying those drugs that may suppress viral replication.

Table: Recommendations for the Use of Drug Resistance Assays*

Clinical Setting/Recommendation	Rationale
Prior to initiating treatment in antiretroviral therapy (ART)-naïve patients, including in the setting of acute human immunodeficiency virus (HIV) infection	Determine if drug-resistant virus was acquired so that an appropriate regimen may be chosen.
Virologic failure during ART	Determine the role of resistance in drug failure, and maximize the number of active drugs in the new regimen.
Suboptimal suppression of viral load after initiation of ART[a]	Determine the role of resistance, and maximize the number of active drugs in the new regimen if indicated.
Not Generally Recommended	
More than 1 year after discontinuation of drugs	Drug-resistance mutations may become minority species in the absence of selective drug pressure and may not be detectable. Current assays may not detect minority drug-resistant species.
Plasma viral load <500 to 1,000 HIV ribonucleic acid (RNA) copies/mL[b]	Resistance assays cannot be reliably performed because of the low copy number of HIV RNA.

*Adapted from the *Department of Health and Human Services (DHHS) Guidelines for the Use of Antiretroviral Agents in HIV-Infected Adults and Adolescents (2006)*

[a]In pregnant women initiating therapy, the clinician may not have as much time to monitor for suboptimal suppression.

[b]The cutoff will vary according to the manufacturer of the kit.

Laboratory Monitoring of ART Side Effects

Bone Marrow Suppression

Complete blood counts should be measured before initiation of ART and at least every 4 months thereafter. For patients at high risk for bone marrow toxicity (e.g., those with advanced HIV infection, those with pre-treatment cytopenias, or those who are receiving zidovudine), blood counts may have to be monitored more frequently because significant cytopenias may occur. (III)

Pancreatitis

When patients receiving ART present with signs and symptoms suggestive of pancreatitis, clinicians should obtain serum amylase and lipase levels. (III)

If signs or symptoms of pancreatitis occur in patients taking antiretroviral medications, the clinician should temporarily suspend the entire ART regimen. A new ART regimen may be initiated when enzymes are normalized but should not include antiretroviral medications that are most likely linked to pancreatitis, such as didanosine or stavudine.

An elevated serum amylase level should be confirmed with a serum lipase level. (III)

Clinicians should not prescribe didanosine for patients who have a history of pancreatitis. (III)

Lactic Acidosis/Hepatic Steatosis

When patients develop symptoms consistent with lactic acidosis syndrome in conjunction with an elevated lactate level (>2 mmol/L) and decreased serum bicarbonate (<20 mmol/L), the clinician should temporarily discontinue the entire ART regimen while an evaluation is conducted. (II)

Routine monitoring of serum lactate levels is not indicated in asymptomatic patients. (I)

Patients who are asymptomatic and have an unexplained decrease in serum bicarbonate level (<20 mmol/L) should be promptly re-evaluated with a repeat test and a venous or arterial lactate. (II) If a venous lactate is mildly elevated (2.1 to 5.0 mmol/L), an arterial lactate should be obtained, and reassessment for the presence of symptoms associated with lactic acidosis should be performed. (I) If the lactate is persistently elevated, the arterial pH is abnormal, or the patient has become symptomatic, ART should be discontinued. (III)

Hepatotoxicity

Clinicians should obtain serum liver enzyme levels at baseline and every 3 to 4 months thereafter in patients receiving ART. (III)

Clinicians should screen for alcohol use in patients with abnormal serum liver enzyme levels. (III)

Use of Nevirapine

Clinicians should not use nevirapine as part of the initial regimen in women with CD4 counts >250 cells/mm^3 or men with CD4 counts >400 cells/mm^3 because of an increased incidence of hepatotoxicity. (I)

When initiating an ART regimen that includes nevirapine, clinicians should obtain serum liver enzymes at baseline, at the time of dose escalation (14 days), and 2 weeks after dose escalation. (III)

Clinicians should counsel patients to seek medical evaluation when signs and symptoms of hepatitis, severe skin reactions, or hypersensitivity reactions related to nevirapine occur. Serum liver enzymes should be obtained whenever patients develop a rash during nevirapine therapy, particularly during the first 18 weeks of therapy. (II)

In the setting of hepatotoxicity related to nevirapine, patients should not be rechallenged with nevirapine. (I)

Renal Toxicity

For All HIV-infected Patients Receiving ART

Clinicians should routinely assess kidney function in all HIV-infected patients. A renal assessment should include:

- Glomerular filtration rate estimated from serum creatinine (baseline and at least every 6 months) (AII)

- Blood urea nitrogen (baseline and at least every 6 months) (AIII)
- Urinalysis (baseline and at least annually) (AIII)
- For patients with diabetes and no known proteinuria: calculation of urine albumin-to-creatinine ratio to detect microalbuminuria (baseline and at least annually) (AI)

For Patients Receiving Tenofovir

For patients initiating a tenofovir-containing regimen, clinicians should calculate glomerular filtration rates at initiation of therapy, 1 month after initiation of therapy, and then at least every 4 months thereafter.

Clinicians should adjust tenofovir dosing when glomerular filtration rate approaches 50 mL/min or discontinue tenofovir according to clinical status. (AII)

For Patients Receiving Indinavir

Clinicians should counsel patients receiving indinavir to drink at least 48 ounces of fluid per day.

Monitoring for Allergic Reactions Associated with ART

When patients receive any new antiretroviral drugs, clinicians should educate them about the possibility of ART-associated allergic reactions, including a hypersensitivity reaction, and the range of possible symptoms (see Table 9 in the original guideline document to view antiretroviral drugs associated with allergic reactions). (III)

Clinicians should discontinue offending drugs when there is a moderate to severe skin reaction, mucous membrane involvement, systemic toxicity, or fever. (I)

Clinicians should perform human leukocyte antigen (HLA) B*5701 testing before initiating abacavir-based therapy.

Clinicians should avoid re-challenging patients with a medication that has been associated with a hypersensitivity reaction, especially in the setting of abacavir reactions and severe NNRTI reactions. (I)

In patients who develop mild rash in response to nevirapine, clinicians should avoid escalating the nevirapine dose to twice daily until after the rash has resolved. For patients with moderate to severe cutaneous toxicity, nevirapine should be discontinued and should not be re-challenged. Use of an alternate NNRTI should be avoided. (III)

Prompt discontinuation of abacavir when a hypersensitivity reaction is suspected is necessary because symptoms will worsen over time. Once abacavir has been discontinued because of a possible or definite hypersensitivity reaction, abacavir should never be administered again. Re-challenge may result in an anaphylactic reaction with associated hypotension or death.

Changing a Successful Initial ART Regimen

Clinicians should change a successful initial ART regimen when the patient's adherence will be compromised by continuing the current regimen. (III)

When considering a change in the ART regime due to drug toxicity, the clinician should confirm that the viral load is maximally suppressed. (III) If maximal viral suppression has been achieved, the clinician should substitute the offending drug. (I)

The clinician should review results from previous resistance testing before changing a successful regimen. (III)

Failure to Achieve Goals of Initial ART

Clinicians should address adherence, obtain resistance assays, and consult with a provider with experience in HIV treatment before changing ART regimens that have failed.

Clinicians should not change an ART regimen when there is incomplete but significant viral suppression (≥0.5 log reduction, or 3-fold, from baseline viral load value) compared with baseline and a more effective ART regimen cannot be constructed as a result of drug resistance or intolerance.

Second-Line Regimens and Salvage ART

Clinicians should consult with a provider with experience in HIV treatment when constructing a second-line regimen and salvage therapy regimens.

Clinicians should review individual antiretroviral history and results from HIV drug resistance testing when constructing salvage therapy regimens. Clinicians should consult with an expert to interpret the results of resistance assays. (I)

Clinicians should use a drug from a class that was not used in the first regimen when constructing a second-line regimen. (I)

When treating patients with high levels of HIV drug resistance, clinicians should consider using agents in novel antiretroviral classes or with unique resistance profiles, such as the entry inhibitors or drugs available through clinical trials or expanded access.

Management of Treatment Interruption

Patients should be discouraged from stopping ART without first consulting with their clinician. (III)

When ART is interrupted, clinicians should inform patients of the potential increased risk of transmitting HIV. Risk-reduction counseling and prevention interventions should be intensified at this time.

Before interrupting ART in patients receiving antiretroviral medications with prolonged half-lives, such as NNRTIs, clinicians should consult with a provider with extensive experience in HIV treatment for guidance on how to avoid the emergence of resistance.

Clinicians should not interrupt lamivudine, emtricitabine, or tenofovir (or combination pills containing these drugs) in patients who are co-infected with chronic hepatitis B without implementing another hepatitis B virus (HBV) treatment option.

Strategic treatment interruption (STI) is not recommended in the management of the HIV-infected patient. (I)

Referring Patients to Research Studies

Referral of patients to research protocols should be 1) to provide treatment or diagnostic options that may be otherwise unavailable and that may enhance treatment outcome, and 2) to attempt to answer a relevant research question. (III)

Patients should be fully informed of any financial benefit their referral to a research study might have for the referring clinician. (III)

Patients should be informed that research studies often require major commitments of time and effort in addition to potential unforeseeable risk. (III)

The clinician should provide assistance to patients who want to participate in research studies. (III)

Definitions:

Quality of Evidence for Recommendations

I. One or more randomized trials with clinical outcomes and/or validated laboratory endpoints
II. One or more well designed, non-randomized trials or observational cohort studies with long-term clinical outcomes
III. Expert opinion

Strength of Recommendation

A. Strong recommendation for the statement
B. Moderate recommendation for the statement
C. Optional recommendation

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

- Human immunodeficiency virus (HIV) infection

- Acquired immunodeficiency syndrome (AIDS)
- Adverse effects of antiretroviral therapy (ART), including:
  - Bone marrow suppression
  - Pancreatitis
  - Lactic acidosis/hepatic steatosis
  - Hepatotoxicity
  - Renal toxicity

Guideline Category

Counseling

Diagnosis

Evaluation

Management

Treatment

Clinical Specialty

Allergy and Immunology

Family Practice

Hematology

Infectious Diseases

Internal Medicine

Obstetrics and Gynecology

Intended Users

Advanced Practice Nurses

Health Care Providers

Pharmacists

Physician Assistants

Physicians

Public Health Departments

Guideline Objective(s)

To provide guidelines for antiretroviral treatment of human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome (AIDS)

Target Population

Human immunodeficiency virus (HIV)-infected patients

Interventions and Practices Considered

1. Inclusion of patient in decision-making
2. Evaluation for initiation of antiretroviral therapy (ART)
    - Assessment of risks and benefits
    - Assessment of patient readiness
    - Assessment of factors that may interfere with treatment
3. Counseling and education
4. Combination of two nucleoside/nucleotide reverse-transcriptase inhibitors (RTIs) plus either a ritonavir-boosted protease inhibitor (PI), a non-nucleoside reverse transcriptase inhibitor (NNRTI), or an integrase strand transfer inhibitors (INSTI)
5. Referrals for
    - Support groups
    - Mental health
    - Drug treatment
6. Follow-up
    - Reinforcement of adherence at regular intervals
    - Genotypic and/or phenotypic testing
    - Regular monitoring of human immunodeficiency virus ribonucleic acid (HIV RNA) levels
    - Avoiding strategic treatment interruption (STI)
7. Monitoring secondary reactions to ART
    - Serum amylase and lipase levels for suspected pancreatitis
    - Serum lactate and serum bicarbonate levels for suspected lactic acidosis or hepatic steatosis
    - Serum liver enzyme levels for suspected hepatotoxicity
    - Kidney function using glomerular filtration rate, blood urea nitrogen, urinalysis, and urine albumin-to-creatinine ratio
8. Changing ART regimens
9. Referral of patients to research studies

Major Outcomes Considered

- Effectiveness of antiretroviral therapy
- Adverse effects of treatment
- Delay in disease progression, prolonged survival, and maintaining quality of life through maximal viral suppression

Methodology

Methods Used to Collect/Select the Evidence

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

The National Library of Medicine, PubMed Central, Cochrane library, and Medline databases were searched for the time frame 2008 to 2013. The inclusion criteria used in the searches were: measurement of effective ART, appropriate frequency of viral load and CD4 count monitoring. The specific search terms used were: ART, adherence, virologic failure, virologic suppression, HIV RNA level, CD4 count, virologic monitoring.

Number of Source Documents

Not stated

Methods Used to Assess the Quality and Strength of the Evidence

Expert Consensus (Committee)

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Quality of Evidence for Recommendation

I. One or more randomized trials with clinical outcomes and/or validated laboratory endpoints
II. One or more well designed, non-randomized trials or observational cohort studies with long-term clinical outcomes
III. Expert opinion

Methods Used to Analyze the Evidence

Systematic Review

Description of the Methods Used to Analyze the Evidence

Not stated

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

AIDS Institute clinical guidelines are developed by distinguished committees of clinicians and others with extensive experience providing care to people with human immunodeficiency virus (HIV) infection. Committees* meet regularly to assess current recommendations and to write and update guidelines in accordance with newly emerging clinical and research developments.

The Committees rely on evidence to the extent possible in formulating recommendations. When data from randomized clinical trials are not available, Committees rely on developing guidelines based on consensus, balancing the use of new information with sound clinical judgment that results in recommendations that are in the best interest of patients.

*Current committees include:

- Medical Care Criteria Committee
- Committee for the Care of Children and Adolescents with HIV Infection
- Dental Standards of Care Committee
- Mental Health Guidelines Committee
- Committee for the Care of Women with HIV Infection
- Committee for the Care of Substance Users with HIV Infection
- Physician's Prevention Advisory Committee
- Pharmacy Advisory Committee

Rating Scheme for the Strength of the Recommendations

Strength of Recommendation

A. Strong recommendation for the statement
B. Moderate recommendation for the statement
C. Optional recommendation

Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

Method of Guideline Validation

External Peer Review

Description of Method of Guideline Validation

All guidelines developed by the Committee are externally peer reviewed by at least two experts in that particular area of patient care, which ensures depth and quality of the guidelines.

Evidence Supporting the Recommendations

References Supporting the Recommendations

Buscher A, Mugavero M, Westfall AO, Keruly J, Moore R, Drainoni ML, Sullivan M, Wilson TE, Rodriguez A, Metsch L, Gardner L, Marks G, Malitz F, Giordano TP. The association of clinical follow-up intervals in HIV-infected persons with viral suppression on subsequent viral suppression. AIDS Patient Care STDS. 2013 Aug;27(8):459-66. PubMed

Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for selected recommendations (see the "Major Recommendations" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Antiretroviral Therapy (ART)

- The preservation and/or restoration of immune function
- Improvement of overall health and the prolongation of life
- The suppression of viral replication
- The possible decrease in risk of viral transmission to others (including fetal transmission)

Early Therapy

- Earlier treatment may reduce both human immunodeficiency virus (HIV)-related and non-HIV-related morbidity and mortality
- Delay or prevention of immune system compromise
- Possible lower risk of antiretroviral resistance
- Decreased risk of sexual transmission of HIV*

*The risk of viral transmission still exists even when the plasma viral load is undetectable; ART is not a substitute for primary HIV prevention measures (e.g., avoiding sharing needles, practicing safer sex).

Potential Harms

Antiretroviral Therapy (ART)

- Adverse effects of the medications on quality of life (for adverse effects and drug interactions of specific antiretroviral drugs, see tables in Appendix A of the original guideline document)
- Known, and as yet unknown, long-term drug toxicities, including potential fetal toxicity
- The development of human immunodeficiency virus (HIV) drug resistance to drugs currently available and possibly to those not yet available, which may limit future treatment options

Early Therapy

- Potential drug-related reduction in quality of life in otherwise asymptomatic individuals
- Possibility of greater cumulative side effects from ART
- Possibility for earlier development of drug resistance and limitation in future antiretroviral options if adherence and viral suppression are suboptimal
- Possibility for earlier onset of treatment fatigue
- Higher prescription drug costs for the individual

Contraindications

Contraindications

- See Table 5-C and Appendix A in the original guideline document for contraindicated combinations of antiretroviral drugs and other medications.
- For women considering pregnancy or likely to become pregnant, efavirenz, or combination pills containing efavirenz, should be avoided. If there are no alternatives for efavirenz in women of childbearing age, clinicians should strongly advise the use of effective contraception and should obtain a pregnancy test before initiation.

Qualifying Statements

Qualifying Statements

When formulating guidelines for a disease as complex and fluid as human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS), it is impossible to anticipate every scenario. It is expected that in specific situations, there will be valid exceptions to the approaches offered in these guidelines and sound reason to deviate from the recommendations provided within.

Implementation of the Guideline

Description of Implementation Strategy

The AIDS Institute's Office of the Medical Director directly oversees the development, publication, dissemination and implementation of clinical practice guidelines, in collaboration with The Johns Hopkins University, Division of Infectious Diseases. These guidelines address the medical management of adults, adolescents and children with human immunodeficiency virus (HIV) infection; primary and secondary prevention in medical settings; and include informational brochures for care providers and the public.

Guidelines Dissemination

Guidelines are disseminated to clinicians, support service providers, and consumers through mass mailings and numerous AIDS Institute-sponsored educational programs. Distribution methods include the HIV Clinical Resource website, the Clinical Education Initiative (CEI), the AIDS Educational Training Centers (AETC), and the HIV/AIDS Materials Initiative. Printed copies of clinical guidelines are available for order from the New York State Department of Health (NYSDOH) Distribution Center.

Guidelines Implementation

The HIV Clinical Guidelines Program works with other programs in the AIDS Institute to promote adoption of guidelines. Clinicians, for example, are targeted through the CEI and the AETC. The CEI provides tailored educational programming on site for health care providers on important topics in HIV care, including those addressed by the HIV Clinical Guidelines Program. The AETC provides conferences, grand rounds and other programs that cover topics contained in AIDS Institute guidelines.

Support service providers are targeted through the HIV Education and Training initiative which provides training on important HIV topics to non-physician health and human services providers. Education is carried out across the State as well as through video conferencing and audio conferencing.

The HIV Clinical Guidelines Program also works in a coordinated manner with the HIV Quality of Care Program to promote implementation of HIV guidelines in New York State. By developing quality indicators based on the guidelines, the AIDS Institute has created a mechanism for measurement of performance that allows providers and consumers to know to what extent specific guidelines have been implemented.

Finally, best practices booklets are developed through the HIV Clinical Guidelines Program. These contain practical solutions to common problems related to access, delivery or coordination of care, in an effort to ensure that HIV guidelines are implemented and that patients receive the highest level of HIV care possible.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Living with Illness

Staying Healthy

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

New York State Department of Health. Antiretroviral therapy. New York (NY): New York State Department of Health; 2014 Jan. 129 p. [106 references]

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2003 Mar (revised 2014 Jan)

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New York State Department of Health - State/Local Government Agency [U.S.]

Source(s) of Funding

New York State Department of Health

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Financial Disclosures/Conflicts of Interest

Not stated

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: New York State Department of Health. Antiretroviral therapy. New York (NY): New York State Department of Health; 2010 Sep. 112 p. [45 references]

Guideline Availability

Electronic copies: Available from the New York State Department of Health AIDS Institute Web site .

Availability of Companion Documents

None available

Patient Resources

None available

NGC Status

This NGC summary was prepared by ECRI on January 21, 2004. This summary was updated by ECRI Institute on February 8, 2005, August 17, 2005, and September 21, 2007. This summary was updated by ECRI Institute on August 11, 2008 following the U.S. Food and Drug Administration advisory on Ziagen (abacavir sulfate). This summary was updated by ECRI Institute on October 8, 2008. This summary was updated by ECRI Institute on January 4, 2010 following the U.S. Food and Drug Administration advisory on Lexiva (fosamprenavir). This summary was updated by ECRI Institute on September 29, 2010. This summary was updated by ECRI Institute on April 13, 2012 following the U.S. Food and Drug Administration advisory on Statins and HIV or Hepatitis C drugs. This summary was updated by ECRI Institute on August 18, 2014.

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